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BEFORE THE SUBCOMMITTEE ON
CRIMINAL JUSTICE, DRUG POLICY AND HUMAN RESOURCES
COMMITTEE ON GOVERNMENT REFORM
UNITED STATES HOUSE OF REPRESENTATIVES

PRESCRIPTION DRUG ABUSE:
WHAT IS BEING DONE TO ADDRESS THIS NEW DRUG EPIDEMIC?

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Mr. Chairman and Members of the Subcommittee, I am Stephen Johnson, Executive Director of Commercial Planning at Pain Therapeutics, Inc. Pain Therapeutics is one of a handful of biopharmaceutical companies in the United States specializing in the research and development of safer drugs for use in pain management, particularly opioid analgesics specially formulated to reduce prescription drug abuse and misuse. We commend the Subcommittee for holding this hearing, and I am grateful for this opportunity to discuss what has become an enormous public health problem. I would like to begin by reviewing the problem of prescription drug abuse, then turn to a brief and non-technical discussion of how novel pharmaceutical technology might address this new drug epidemic. I will then close with four recommendations for your review and consideration.

As this Subcommittee knows all too well, prescription drug abuse continues to have a widespread and devastating effect on American families, businesses, and our society as a whole.

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Non-medical use of prescription drugs is the second-most prevalent category of drug abuse, after marijuana.[1] In fact, 56 percent more Americans abuse prescription drugs than abuse cocaine, heroin, hallucinogens, and inhalants – combined.[2] Among teenagers, the problem of prescription drug abuse is even more worrisome. According to recent data published by the Partnership for a Drug-Free America, 19 percent of children ages 12 to 17 report having abused prescription drugs, of which the largest category is pain relievers.[3]

Prescription drug abuse inflicts enormous costs on our society. In 2002 alone, abuse of prescription drugs cost Americans nearly $181 billion.[4] Direct costs related to non-medical use of prescription drugs are considerable – for example, 25 percent of visits to hospital emergency departments are associated with abuse of prescription drugs.[5] Indirect costs result from drug theft, the commission of crimes to support addiction, "doctor shopping," lost productivity and wages, and the administration of law enforcement.

The largest group of prescription drug abusers is comprised of individuals who abuse opioids,[6] a class of drugs widely prescribed to treat pain. Examples of prescription opioid drugs include oxycodone, hydrocodone, morphine, and fentanyl. When both appropriately prescribed by a physician and used properly by a patient, opioid drugs can manage pain, especially severe chronic pain due to cancer, failed back syndrome, or advanced forms of arthritis. When abused, however, opioid drugs can also induce some sort of extreme euphoria. Chronic drug abusers will repeatedly pursue the experience of such euphoria without regard for their well-being or the welfare of others. Interestingly, there currently is no way to predict which patients will end up abusing opioid drugs. Moreover, just this week, researchers at the Centers for Disease Control and Prevention published a study revealing that opioids account for more overdose deaths in the United States than either heroin or cocaine.[7] For these reasons, and many others, I believe the pharmaceutical industry must have a leadership role in preventing the abuse and misuse of opioid drugs.

For abusers, the appeal of a prescription drug typically depends on its dose strength and the ease with which it can be abused. Illustrative is OxyContin®, a strong, oral opioid drug typically prescribed to treat moderate to severe pain. Unfortunately, it is also reported to be one of the most commonly abused, branded, prescription controlled substances in the United States. The active ingredient in OxyContin® is oxycodone, a potent opioid which is a Schedule II controlled substance because it has an abuse liability similar to morphine. OxyContin® contains a very high dose of oxycodone that, when used properly, is intended to be slowly released over 12 hours. Drug abusers, however, can quickly and simply disable OxyContin's® controlled release mechanism – usually by crushing, breaking, or chewing a tablet, or by stirring it in high-proof alcohol for a few minutes. The extracted oxycodone is then ingested, snorted, or injected, immediately releasing into the body a dose of drug that was intended to be slowly delivered over a 12-hour period. The ease of abuse, combined with the potency of the active drug ingredient, allows drug abusers to experience a very powerful and immediate high

According to the Drug Enforcement Administration (DEA), criminal activity related to OxyContin® abuse and diversion is rapidly depleting the resources of law enforcement.[8] In fact, DEA reports record the theft of 1,369,667 dosage units of OxyContin® between January 2000 and June 2003.[9] Moreover, fully 25 percent of the Schedule II investigations conducted by DEA between Fiscal Year (FY) 2001 and FY 2003 involved OxyContin®.[10]

While urgent action is needed to more adequately address this epidemic, it is also critically important that any efforts to prevent prescription drug abuse not unduly restrict appropriate access to effective pain therapies for the patients who need them. In fact, pain already is too often undertreated.[11] Unfortunately, criminal and civil liability and theft associated with OxyContin® are discouraging some doctors from prescribing the pain treatments their patients need, and dissuading some pharmacists from stocking them.

Under the Controlled Substances Act (CSA), DEA is responsible for maintaining a closed system of distribution for controlled substances by administering stringent requirements applicable to manufacturers, distributors, physicians, and pharmacists.[12] Such requirements include registration, recordkeeping, reporting, security, scheduling, production quotas, and import/export authorization. Over the years, these controls have been particularly effective in dramatically reducing diversion at the manufacturer and distributor level, a significant source of diversion when the CSA was passed. However, traffickers and abusers currently divert Schedule II opiates from the retail level (physicians and pharmacists), where the federal government has less control. Currently, Federal efforts to address prescription drug abuse principally rely on costly and sustained risk management approaches, including: physician and patient education, surveillance of the distribution and dispensing of controlled substances, marketing restrictions, warning labels, and law enforcement.

Unfortunately, despite the tireless efforts of thousands of Federal, State, and local officials working to implement these practices, as well as the enormous financial resources appropriated to support them, the incidence of prescription drug abuse has continued to rise – even as the rate at which other categories of illicit drug use have decreased or remained stable.[13] In fact, the number of Americans abusing prescription drugs rose 94 percent between 1992 and 2003, a period during which the U.S. population increased only 14 percent.[14] Moreover, during the same period, there was a 212 percent increase in the number of children ages 12 to 17 abusing prescription drugs, and, remarkably, a 542 percent increase in teens initiating abuse of prescription opioids.[15] Notably, approximately 600,000 Americans became new abusers of OxyContin® in 2004 alone.[16] Clearly, additional methods of combating prescription drug abuse are necessary.

At Pain Therapeutics, we believe that the battle against prescription drug abuse is a shared responsibility among government, the healthcare community, and the pharmaceutical industry. The

use of novel pharmaceutical technology can help combat the problem of prescription drug abuse. In fact, our scientists are using innovative chemical advances to develop a tamper-resistant capsule that provides long-acting, effective pain relief when used properly, while also resisting degradation under conditions of abuse.

For example, our investigational drug product Remoxy™ is a novel form of long-acting oxycodone. The capsule, which contains oxycodone in a highly viscous fluid, is formulated to be resistant to tampering or accidental misuse. While Remoxy™ is not intended to be abuse-proof – a sophisticated chemical laboratory might still manage to extract its active ingredient – it cannot be readily broken, chewed, or crushed, which are the principal means by which abusers disable the extended release mechanism of OxyContin® and other sustained release opioid drug products. Importantly, although the labeling for Remoxy™ will ultimately be determined in the course of Food and Drug Administration (FDA) review, we believe this investigational drug will also reduce the potential for accidental overdose, which too often occurs when elderly patients and others who find an OxyContin® tablet difficult to swallow ingest its contents after crushing, breaking, or chewing it. Moreover, we expect Remoxy's™ advanced technology to be useful in reformulating other commonly abused opioid drug products to similarly render them abuse-resistant. Remoxy™ is currently in late-stage testing in nearly 40 clinical sites across the United States. We hope to be able to file for approval to market this novel formulation in late-2007.

We are taking a very different approach to reducing prescription drug abuse in developing Oxytrex™, an investigational drug product that combines oxycodone, an opioid agonist, with an ultra-low-dose of an opioid antagonist. Research has shown that the addition of an ultra-low-dose opioid antagonist blocks activation of the body's excitatory opioid receptors, while allowing the agonist to block the transmission of pain signals.[17] We are working to demonstrate that Oxytrex™ can significantly inhibit pain while simultaneously reducing the risk of physical dependence, which is

a physiological adaptation to the continued use of a drug that can often lead to both a diminished physiological sensitivity to the drug's effects (tolerance) and adverse physical symptoms upon withdrawal of the drug's use.

We believe that prescription drugs that are specially formulated to reduce the risk of abuse can significantly contribute to current efforts to address the nation's prescription drug abuse epidemic. Importantly, abuse resistant prescription drugs could also diminish the burden on law enforcement. Additionally, the development of such products represents a new and efficient means of addressing Congress' increasing concern regarding prescription drug safety, and could do so without further restricting or discouraging access for patients who need such care. In fact, the availability of such products could enhance appropriate prescribing of opioid drugs by diminishing the stigma associated with commonly abused drugs and reducing the threat of civil and criminal liability that can discourage physicians from prescribing more readily abused prescription controlled drugs.

Pain Therapeutics is not alone in recognizing the potential benefits of formulating prescription drugs to reduce abuse. In fact, several governmental entities and organizations have been urging the development of abuse-resistant prescription drugs. For example, over the past several years, DEA has repeatedly indicated that it is working closely with the FDA "to strongly urge the rapid reformulation of OxyContin by Purdue Pharma, to the extent that is technically possible, in order to reduce the abuse of the product, particularly by injection."[18] Additionally, the FY 2006 House Appropriations Committee report notes that "[p]roviders and patients alike will benefit from the expedited review of safer drugs, as well as the provision of information that accurately differentiates abuse-resistant formulations."[19] Meanwhile, the corresponding House-Senate Conference report advises that "new drug applications and supplements seeking approval for replacement or alternative abuse-resistant formulations of currently available drug products that

include an active ingredient that is a listed chemical under the Controlled Substances Act . . . may be considered under the expedited, priority review process at FDA."[20]

Further, the 2006 "Synthetic Drug Control Strategy" issued by the Office of National Drug Control Policy lists as its third of 46 recommendations: "Continue to support the efforts of firms that manufacture frequently diverted pharmaceutical products to reformulate their products so as to reduce diversion and abuse."[21] A comprehensive report issued in 2005 by the National Center on Addiction and Substance Abuse at Columbia University goes even further, urging:

> The FDA should require pharmaceutical companies manufacturing controlled drugs to formulate or reformulate the drugs where possible to minimize the risk of abuse. Pharmaceutical companies should be required to demonstrate in their application materials for FDA approval of new drugs that they have made every effort to formulate the drug in such a way that avoids or at least minimizes the drug's potential for abuse.[22]

Earlier this year, National Institute on Drug Abuse Director Dr. Nora Volkow coauthored a paper on opioid analgesic abuse calling for development of "less abusable, but still potent, forms of opioid agents," as well as "combinations of medications that can be given to treat pain but to minimize the chances of addiction."[23]

Now we must turn these statements into real public health and law enforcement achievements. Currently, there are no Schedule II prescription controlled drugs on the market specifically formulated to resist or reduce abuse. No trailblazer exists to guide industry in determining whether and how to pursue development of such products. Moreover no statute, regulation, or administrative guidance specifically addresses issues that are critical to determining whether it will continue to be worthwhile to invest in the research and development to bring such products to market. This Subcommittee can play a unique role in ensuring that agencies across the government coordinate their efforts to maximize the benefits of pharmaceutical technology in addressing drug abuse and misuse.

We recommend the following:

1. Applications to market prescription drugs that are specially formulated to deter abuse or misuse should be eligible for priority review.
2. FDA should permit labeling that accurately conveys the specific means of abuse or misuse to which a product has been shown to be resistant; and the agency should not require companies to demonstrate resistance to all potential methods of abuse and misuse, such as those that are relatively uncommon.
3. Risk management plans for abuse-resistant products should reflect their inherent safeguards. Appropriate risk management plans could encourage physicians to prescribe those products that deter abuse and misuse, while also discouraging use of prescription drugs known to be readily abusable.
4. We must recognize that achieving approval and meaningful labeling for these products will be a pyrrhic victory if patients are not given access to products incorporating abuse- and misuse-resistant technologies. Given the cost of prescription drug abuse and misuse to our healthcare system, we must ensure that both private and governmental payors, such as Medicare Part D plans and the Medicaid program, recognize the benefits of these products, and favor their use in their formularies.

As a first step, we welcome FDA's recent announcement that it intends to develop this year guidance for industry on both "Assessment of Abuse Potential of Drugs"[24] and "Developing Analgesic Products for the Treatment of Pain,"[25] and we are hopeful that the prompt issuance of these documents will eliminate some of the current ambiguity that may be discouraging development of prescription drugs formulated for reduced abuse potential. We hope such guidance will seek to encourage the development of abuse-resistant prescription drugs by instituting

reasonable standards for accurate labeling that clearly differentiates products incorporating such technologies from products providing no abuse- or misuse-deterrent benefit.

Mr. Chairman, we are especially grateful to you and the other Members of the Subcommittee for calling attention to this issue today. Pain Therapeutics looks forward to working with Congress, FDA, DEA, and other government agencies to continue to promote the development of innovative approaches to more effectively address the epidemic of prescription drug abuse.

Thank you. I would be pleased to answer any questions.

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[1] Substance Abuse and Mental Health Services Administration, Office of Applied Studies, *Results from the 2005 National Survey on Drug Use and Health: National Findings*, DHHS Pub. No. SMA 05-4062, at 232 (Sept. 8, 2005).
[2] *Id.*
[3] The Partnership for a Drug-Free America, *The Partnership Attitude Tracking Study (PATS): Teens in Grades 7 through 12*, at 21 (May 2006).
[4] Office of National Drug Control Policy, *The Economic Costs of Drug Abuse in the United States, 1992-2002*, Pub. No. 207303, at vi (Dec. 2004).
[5] Substance Abuse and Mental Health Services Administration, Office of Applied Studies, Drug Abuse *Warning Network, 2004: National Estimates of Drug-Related Emergency Department Visits*, DHHS Pub. No. (SMA) 06-4143, at 21 (Apr. 2006).
[6] The National Center on Addiction and Substance Abuse, *Under the Counter: The Diversion and Abuse of Controlled Prescription Drugs in the U.S*. 32 (July 2005) *available at* http://www.casacolumbia.org/absolutenm/articlefiles/380-under_the_counter_-_diversion.pdf (last viewed July 23, 2006).
[7] Opiate Painkiller ODS Now Top Those for Cocaine, Heroin, Forbes On-Line (July 24, 2006) *available at* http://www.forbes.com/forbeslife/health/feeds/hscout/2006/07/24/hscout533964.html (last viewed July 24, 2006).
[8] Drug Enforcement Administration, Office of Diversion Control, *Action Plan to Prevent the Diversion and Abuse of OxyContin®*, *available at* http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/abuse_oxy.htm (last viewed July 23, 2006).
[9] Office of National Drug Control Policy, *Drug Fact Sheet: OxyContin* (last updated June 16, 2006) *available at* http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/abuse_oxy.htm (last visited July 23, 2006).
[10] *Overview of the President's Fiscal Year 2007 Request for the Dep't of Justice: Hearing Before the Subcomm. on Commerce, Justice and Science of the Senate Comm. On Appropriations*, 109th Cong. (Apr. 5, 2006) (attachment accompanying statement of Karen P. Tandy, Administrator, Drug Enforcement Admin.) *available at* http//www.usdoj.gov/dea/pubs/cngrtest/ct040506_attachp.html (last viewed July 23, 2006).
[11] *See, e.g., OxyContin and Beyond: Examining the Role of FDA and DEA in Regulating Prescription Painkillers: Hearing Before the Subcomm. on Regulatory Affairs of the House Comm. On Government Reform*, 109th Cong. 26-27 (2005) (statement of Robert J. Meyer, Director, Off. of Drug Evaluation II, Center for Drug Evaluation & Research, Food & Drug Admin.).
[12] 21 U.S.C. § 802 (2001).
[13].*See, e.g., OxyContin and Beyond: Examining the Role of FDA and DEA in Regulating Prescription Painkillers: Hearing Before the Subcomm. on Regulatory Affairs of the House Comm. On Government Reform*, 109th Cong. 27 (2005) (statement of Robert J. Meyer, Director, Off. of Drug Evaluation II, Center for Drug Evaluation & Research, Food & Drug Admin.)

[14] The National Center on Addiction and Substance Abuse, *Under the Counter: The Diversion and Abuse of Controlled Prescription Drugs in the U.S.*, at i (July 2005) *available at* http://www.casacolumbia.org/absolutenm/articlefiles/380-under_the_counter_-_diversion.pdf (last viewed July 23, 2006).
[15] *Id.*
[16] Substance Abuse and Mental Health Services Administration, Office of Applied Studies, *Results from the 2005 National Survey on Drug Use and Health: National Findings*, DHHS Pub. No. SMA 05-4062, at 50 (Sept. 8, 2005).
[17] Lynn R. Webster et al., *Oxytrex Minimizes Physical Dependence While Providing Effective Analgesia: A Randomized Controlled Trial in Low Back Pain*, J. Pain (forthcoming 2006); Walter Ling et al., *Abuse of Prescription Opioids*, *in* Principles of Addiction Medicine (Allan W. Graham et al. eds., 2003).
[18] *See, e.g.,* Drug Enforcement Administration, Office of Diversion Control, *Action Plan to Prevent the Diversion and Abuse of OxyContin®*, *available at* http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/abuse_oxy.htm (last viewed July 23, 2006); Drug Enforcement Admin., Office of Diversion Control, OxyContin®: Diversion & Abuse, at 9 (Oct. 2003) *available at* http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/oxy_oct2003.pdf (last viewed July 23, 2006).
[19] H.R. Rep. No. 109-102, at 81 (2005).
[20] H.R. Rep. No. 109-255, at 102 (2005).
[21] Office of National Drug Control Policy, *Synthetic Drug Control Strategy: A Focus on Methamphetamine and Prescription Drug Abuse* 44 (2006) *available at*
http://www.whitehousedrugpolicy.gov/publications/synthetic_drg_control_strat/synth_strat.pdf.
[22] The National Center on Addiction and Substance Abuse, *Under the Counter: The Diversion and Abuse of Controlled Prescription Drugs in the U.S.*, at 101-102 (July 2005) *available at* http://www.casacolumbia.org/absolutenm/articlefiles/380-under_the_counter_-_diversion.pdf (last viewed July 23, 2006).
[23] Wilson M. Compton and Nora D. Volkow, *Major Increases in Opioid Analgesic Abuse in the United States: Concerns and Strategies*, 81 Drug & Alcohol Dependence 103, 106 (2006).
[24] Center for Drug Evaluation & Research, Food & Drug Admin., *Guidance Agenda: Guidances CDER Is Planning to Develop During Calendar Year 2006* (2006) *available at* http://www.fda.gov/cder/guidance/CY06.pdf (last viewed July 23, 2006).
[25] *Id.*